

## **ATTORNEY DOCKET NO. 50304/114001**

Certificate of Mailing: Date of Deposit: May 16, 2007
I hereby certify under 37 C.F.R. § 1.8(a) that this correspondence is being deposited with the United States Postal Service as <b>first class mail</b> with sufficient postage on the date indicated above and is addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
Megan Kiley Printed name of person mailing correspondence Signature of person mailing correspondence

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

Waer et al.

Confirmation No.: 3570

Serial No.:

10/595,161 /

Art Unit:

2621

Filed:

March 10, 2006

Examiner:

Not Yet Assigned

Customer No.:

21559

Title:

PTERIDINE DERIVATIVES FOR THE TREATMENT OF SEPTIC

SHOCK AND TNF-α-RELATED DISEASES

Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

## SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Applicants submit the references listed on the enclosed Form PTO-1449, copies of which are enclosed, with the exception of U.S. patents and U.S. patent application publications.

Submission of this statement is not a representation that a search has been made, nor is the inclusion of information in this statement an admission that the information is material to patentability.

This statement is being filed before the receipt of a first Office action on the merits.

If there are any charges or any credits, please apply them to Deposit Account . No. 03-2095.

Respectfully submitted,

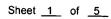
J. Cooper McDonald, Ph.D. Reg. No. 52,011

James D. DeCamp, Ph.D. Reg. No. 43,580

Clark & Elbing LLP 101 Federal Street Boston, MA 02110

Telephone: 617-428-0200 Facsimile: 617-428-7045

2





INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use several sheets if necessary)

SUBSTITUTE FORM PTO-1449 (MODIFIED)

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

Attorney Docket No.

50304/114001

Serial No.

10/595,161

Applicant

Waer et al.

Filing Date

March 10, 2006

Group

2621

(37 C.F.R. § 1.98(b))

**IDS Filed** 

May 16, 2007

U.S. PATENT DOCUMENTS						
Examiner's Document Finitials Number		Publication/ Issue Date	Patentee or Applicant	Class	Subclass	Filing Date (If Appropriate)
	2003/236255	12-25-2003	Waer et al.			
	2,512,572	06-20-1950	Smith, Jr. et al.			
	2,581,889	01-08-1952	Timmis			
	2,665,275	01-05-1954	Campbell et al.			
	2,667,486	01-26-1954	Cain			
	2,740,784	04-03-1956	Sletzinger et al.			
	2,940,972	06-14-1960	Roch			
	3,071,587	01-01-1963	Curran			
	3,081,230	03-12-1963	Weinstock et al.			
	3,159,628	12-01-1964	Pachter et al.			
	3,475,425	10-1969	Roch, Joseph			
	3,859,287	01-07-1975	Parish et al.			
	5,665,772	09-09-1997	Cottens et al.			
	5,780,462	07-14-1998	Lee et al.			
	5,843,943	12-1-1998	Carson et al.			
	5,992,713	11-30-1999	Manabat			
	6,331,547	12-18-2001	Zhu et al.			
	6,440,991	08-27-2002	Zhu et al.			
	2006/0189620	8-24-2006	Waer et al.			
	2007/0043000	2-22-2007	Waer et al.			

EXA	ιлл	INI	$-\nu$

DATE CONSIDERED

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.

	Sheet 2 of 5
Attorney Docket No.	50304/114001
Serial No.	10/595,161
Applicant	Waer et al.
Filing Date	March 10, 2006
Group	2621
IDS Filed	May 16, 2007
	Serial No. Applicant Filing Date Group

 U.S. PATENT DOCUMENTS							
2006/0287314	12-21-2006	Waer et al.					
2007/0032477	02-08-2007	Waer et al.					
 6,946,465	09-20-2005	Waer et al.					

FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION						
Examiner's Initials	Document Number	Publication or Issue Date	Country or Patent Office	Class	Subclass	Translation (Yes/No)
	CH 231,852	07-17-1944	Switzerland			
	DE 19 21 308	01-07-1971	Germany			
	DE 40 09 941	10-02-1991	Germany			-
	EP 0 108 890	05-23-1984	EPO			
	EP 0 134 922	03-27-1985	EPO			
	EP 0 185 259	06-25-1986	EPO			
	EP 0 956 855	11-17-1999	EPO			
	EP 1 479 682	11-24-2004	EPO			
	EP 0 574 906	12-22-1993	EPO			
	GB 2 405 793	03-16-2005	United Kingdom			
	GB 677,342	08-13-1952	United Kingdom			
	GB 763,044	12-05-1956	United Kingdom			
	GB 785,353	10-30-1957	United Kingdom			
	WO 00/45800	08-10-2000	WIPO			
<del>-</del>	WO 01/19825	03-22-2001	WIPO			

EX	4Mil	NEK	

DATE CONSIDERED

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.

SUBSTITUTE FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE	Attorney Docket No.	50304/114001
(MODIFIED)	PATENT AND TRADEMARK OFFICE		10/595,161
INFORMATIO	ON DISCLOSURE	Applicant	Waer et al.
STATEMEN	T BY APPLICANT sheets if necessary)	Filing Date	March 10, 2006
	,,	Group	2621
(37 C.F.R. § 1.98(b))		IDS Filed	May 16, 2007

FOF	FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION						
WO 94/11001	05-26-1994	WIPO					
WO 94/06431	03-31-1994	WIPO					
WO 95/31987	11-30-1995	WIPO					
WO 95/32203	11-30-1995	WIPO					
WO 98/04558	02-5-1998	WIPO	-				
WO 98/08516	03-5-1998	WIPO					
WO 98/52948	11-26-1998	WIPO					
WO 04/104005	12-02-2004	WIPO					
WO 05/021003	03-10-2005	WIPO					
WO 05/039587	05-06-2005	WIPO					

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)
Baba et al., "Synergistic Antiviral Effects of Antiherpes Compounds and Human Leukocyte Interferon on Varicella-Zoster Virus in Vitro," <i>Antimicrob. Agents Chemother.</i> 25:515-517 (1984).
Beilstein search, XP-002324247.
Beilstein Database, Beilstein Institute For Organic Chemistry 28:1015-1020 (1992), XP-002296933.
Beilstein Database, Beilstein Institute For Organic Chemistry 90:2631, 2633, 2635 (1957) XP-002296934.
Beilstein Database, Beilstein Institute For Organic Chemistry 93:2668, 2671 (1960) XP-002296935.
 Beilstein Database, Beilstein Institute For Organic Chemistry 52:1403-1410 (2003) XP-002296936.
 Beilstein Database, Beilstein Institute For Organic Chemistry 41:781-788 (1995) XP-002296937.
 Beilstein Database, Beilstein Institute For Organic Chemistry 48:1255-1274 (1998) XP-002296938.
Black et al., "Agents that Block TNF-ą Synthesis or Activity," Ann Rep. Med. Chem. 32:241-250 (1997).
Boon, "Pteridines. Part IV.* Derivatives of 2:4-Diaminopteridine and Related Compounds," <i>J. Chem. Soc.</i> 2146-2158 (1957).

EXAMINER	DATE CONSIDERED
EXAMINER: Initial citation considered. Draw line through citation form with the next communication to applicant.	n if not in conformance and not considered. Include copy of this

	SUBSTITUTE FORM PTO-1449			50304/114001
	(MODIFIED) PATENT AND TRADEMARK OF		Serial No.	10/595,161
	INFORMATIO	ON DISCLOSURE	Applicant	Waer et al.
	STATEMENT	F BY APPLICANT heets if necessary)	Filing Date	March 10, 2006
	(OSC SCVCIAI S	need ii needssaiy)	Group	2621
٠	(37 C.F.R. § 1.98(b))		IDS Filed	May 16, 2007
Į				

FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION
Cairo, "Immunology Lecture #20 Transplantation Immunology," Columbia University, [online] (2003).
Chantry "Emerging Drugs: The Prospect for Improved Medicines," 1:5-13 (1999).
Chou and Talalay, "Quantitative Analysis of Dose-Effect Relationships: The Combined Effects of Multiple Drugs or Enzyme Inhibitors," <i>Adv. Enzyme Regul.</i> 22:27-55 (1984).
Cottam et al., "Substituted Xanthines, Pteridinediones and Related Compounds as Potential Anti-Inflammatory Agents. Synthesis and Biological Evaluation of Inhibitors of Tumor Necrosis Factor alpha.," <i>J. Med. Chem.</i> 39:2-9 (1996).
Elion et al., "Antagonists of Nucleic Acid Derivatives. VIII. Synergism in Combinations of Biochemically Related Antimetabolites," <i>J. Biol. Chem.</i> 208:477-488 (1954).
Elliott et al., "Synthesis of N-10-Methyl-4-Thiofolic Acid and Related Compounds," <i>Journal of Medicinal Chemistry</i> 18:492-496 (1975).
Giori et al., "Reactivity of 3H-Pyrimido[5, 4-c] [1, 2, 5] Oxadiazin-3-one Towards Carbanions: Synthesis of Pteridine-2, 4-Diones," <i>J. Heterocyclic Chemistry</i> 23:1661-1665 (1986).
Illei and Lipsky, "Novel, non-Antigen-Specific Therapeutic Approaches to Autoimmune/Inflammatory Diseases," Current Opinion in Immunology 12:712-718 (2000).
Israel et al., "Pyrimidine Derivatives. VII. Some Condensed Derivatives of 2, 4, 5-Triamino-6-Methylthiopyrimidine," <i>Journal of Pharmaceutical Sciences</i> 54:1626-1632 1965.
Kaldrikyan, M.A. et al., "Pteridine Derivatives. I. Synthesis of Some Substituted 6,7-Diarylpteridines," <i>Armyanskii Khimicheskii</i> Zhurnal 29:337-341 (1976) (abstract only)
Landauer and Rydon, "A Convenient Synthesis of Some 4-Substituted 5-Aminopyrimidines," J. Chem. Soc. 3721-3722 (1953).
Lin et al., "Use of the Methylxanthine Derivative A802715 in Transplantation Immunology, I. Strong in Vitro Inhibitory Effects on CD28-Costimulated T Cell Activities," <i>Transplantation</i> 63:1813-1819 (1997).
Lin et al., "Use of the Methylxanthine Derivative A802715 in Transplantation Immunology, II. In Vivo Experiments," <i>Transplantation</i> 63:1734-1738 (1997).
Merz et al., "Synthesis of 7-Benzylamino-6-chloro-2-piperazino-4-pyrrolidinopteridine and Novel Derivatives Free of Positional Isomers. Potent Inhibitors of cAMP-Specific Phosphodiesterase and of Malignant Tumor Cell Growth," <i>J. Med. Chem.</i> 41:4733-4743 (1998).
Mohr et al., "Pteridines: Synthesis and Properties of 6-Thioxanthopterin and 7-Thioisoxanthopterin," Helv. Chim. Acta 75:2317-2326 (1992).

EXAMINER	DATE CONSIDERED			
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.				

SUBSTITUTE FORM PTO-1449 (MODIFIED)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	Attorney Docket No.	50304/114001
(WODIFIED)		Serial No.	10/595,161
INFORMATION	ON DISCLOSURE	Applicant	Waer et al.
STATEMEN'	T BY APPLICANT sheets if necessary)	Filing Date	March 10, 2006
(230 30 13 14)	ii	Group	2621
(37 C.F.R. § 1.98(b))		IDS Filed	May 16, 2007

FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION
Murata et al.,"A Facile Method for Regioselective 6,7-Disubstitution of Pteridine," <i>Heterocycles</i> 53:1259-1262 (2000).
Pfleiderer and Lohrmann, "Pteridine, XII: Synthese von 2-Amino-4-Alkoxy-Pteridinen," Chem. Ber. 94:12-18 (1961).
Sato and Fukuya, "Studies on Pyrazines. Part 37. <sup>1</sup> Synthesis of 6-Propionylpteridine-2,4 (1H,3H)-dione and its 1-and/or 3-Methyl Derivatives from Marine Natural Products," J. Chem. Soc., Perkin Trans. 1:89-95 (2000).
Spickett et al., "The Synthesis of Compounds With Potential Anti-Folic Acid Activity. Part I. 7-Amino- And 7-Hydroxy-Pteridines," <i>Journal of The chemical Society, Chemical Society. Letchworth</i> 2887-2891 (1954).
Weinstock et al., "Pteridines. XII. Structure-Activity Relationships of Some Pteridine Diuretics," <i>J. Med. Chem.</i> 11:573-579 (1968).
West, "Chapter 10 Solid Solutions: Solid State Chemistry and its Applications," Wiley 358 & 365 (1988).
Yao and Pfleiderer, "Pteridines. Protection of Pteridines", Helvetica Chimica Acta, 86:1-12 (2003).
Neilsen et al., "Unequivocal syntheses of 6-methyl- and 6-phenylisoxanthopterin" J. Heterocyclic Chem., 24, 1621-1628 (1987)
Taghavi-Moghadam et al., "A new, general, and regioselective method for the synthesis of 2, 6-disubstituted 4-aminopteridines", <i>Tetrahedron Lett.</i> , 38 (39), 6835-6836 (1997)
Jackson et al., "6, 7-disubstituted 2, 4-diaminopteridines: novel inhibitors of <i>Pneumocystis carinii</i> and <i>Toxoplasma gondii</i> dihydrofolate reductase", <i>Antimicrobial Agents and Chemotherapy</i> , 40:1371-1375 (1996)
Magnus et al. "Neural stem cells in inflammatory CNS diseases: mechanisms and therapy" J. Cell. Mol. Med. 2005, 9:303-319.
Obach "Drug-drug interactions: an important negative attribute in drugs" Drugs of Today 2003, 39:301-338.
Cecil Textbook of Medicine, 20 <sup>th</sup> edition (1996), Section Five- Degenerative Diseases of the Nervous System, vol. 2, pp:2050-2057.
Cecil Textbook of Medicine, 20 <sup>th</sup> edition (1996), vol. 2, pp:1992-1996.
"FDA mulls drug to slow late-stage Alzheimer's" cnn.com 9/24/2003.
Wikipedia entries for Antihistamine, Autoimmunity, List of autoimmune diseases, Lupus erythematosus, and Sjogren's syndrome, printed from http://en.wikipedia.org on December 28, 2006.

EXAMINER	DATE CONSIDERED		
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.			